Biological Adaptive Protection Notes

This presentation addresses biological adaptive protection, which is the physiological expression of cellular capabilities to maintain tissue structure integrity and function when exposed to low levels of potentially harmful agents – in this case from ionizing radiation.

Slide 2 – adaptive protection graphic

- adaptive protection activated when cell exposed to potentially damaging stressors
- molecular and DNA damage may be linear function of radiation dose, but biological response to damage not linear
- elimination, modulation, and propagation of damage are normal biological responses to encountered stressors
- system modulation response refers to
  - regulation of biological changes within specific limits,
  - adjusting biological environment to correct undesired change, or
  - adapting to a new biological environment created by change
- phenotype alterations – observable, physical, or biochemical changes resulting from biological response to encountered stressors
- linear no-threshold (LNT) dose-response model ignores body's highly effective adaptive protection mechanisms

Slide 4 – DNA damage repair mechanisms

- graphic illustrates four types of DNA damage agents (i.e., stressors), five DNA damage types, and the associated repair mechanisms
- ionizing radiation only one of potential damaging agents
- single strand breaks, induced by reactive oxygen species (ROS), constitutes overwhelming majority of DNA phenotype alterations

Slide 5 – dual effect of radiation graphic

- figure illustrates non-linearity of adaptive protection response to radiation-induced stress
- acute radiation doses up to ≈0.2 Gy stimulate adaptive protection mechanisms and cell "repair centers" correctly repair DNA damage
- 0.1 Gy dose reasonable approximation for maximal adaptive protection stimulation
- 0.2 Gy dose reasonable approximation for high dose threshold – also known as no observed adverse effect level (NOAEL) or zero equivalent point (ZEP)

- high doses inhibit adaptive protection mechanisms; for high doses >0.6 Gy repair process challenged, repair error rate increases, and cancer risk association with dose becomes linear
- ref. point – chest x-ray is thousand times smaller (0.0001 Gy) than optimum dose

Slide 10 – adaptive protection mechanisms graphic

- complex system evolved in aerobic organisms over eons of time to control enormous, relentless burden of DNA alterations produced by ROS, generated principally by free radicals created from mitochondrial oxygen metabolism
- adaptive protection sequentially reduces DNA damage from about one million DNA alterations/cell/day to about one "mutation"/cell/day
- first bar – daily rate of free radical production in human cells with **potential** to cause DNA damage
- second bar – cell antioxidants neutralize metabolism-induced free radicals, reducing **potential** for DNA damage by factor of 1,000
- third bar – cell enzymes repair some DNA damage, reducing actual damage by factor of 10,000
- fourth bar – approximately 99% of unrepaired DNA permanently removed from cell
- parentheticals indicate rate of metabolism-induced DNA damage about 7 orders of magnitude higher than rate of radiation-induced DNA damage due to daily low LET background radiation dose of about 2.7 μGy (same as 0.1 cGy/y) Note that average U.S. daily exposure from natural background radiation is ≈10 μGy.